PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RJS/B45331	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/14562	International filing date *(day/month/year)* 18.12.2003	Priority date *(day/month/year)* 20.12.2002
International Patent Classification (IPC) or both national classification and IPC A61K39/12		
Applicant GLAXOSMITHKLINE BIOLOGICALS SA et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30.06.2004	27.01.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Lechner, O Telephone No. +49 89 2399-8687

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/14562

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-23 as originally filed

Claims, Numbers

1-21 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 5, 6, 11-20 (all in part)

   because:

   ☒ the said international application, or the said claims Nos. 11-19 (all in part) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 5, 6, 19, 20 (all in part) are so unclear that no meaningful opinion could be formed *(specify)*:

   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-20
	No:	Claims	21
Inventive step (IS)	Yes:	Claims	1-20
	No:	Claims	21
Industrial applicability (IA)	Yes:	Claims	
	No:	Claims	see sep-sheet

2. Citations and explanations

   see separate sheet

item III

1 **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability (Rule 67.1, PCT)**

For the assessment of the present **claims 11-19** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claims 11-19 relate to subject matter considered by this Authority to be covered by the provisions of **Rule 67.1(iv), PCT**. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims **(Article 34(4)(a)(I), PCT)**.

2 **Major clarity problems (Article 6, PCT)**

2.1 **Claims 6, 19** and **20** do not meet the requirements of **Article 6, PCT** in that the matter for which protection is sought is not clearly defined. The claim/s attempt/s to define the subject-matter in terms of the result to be achieved which, i.e. "prevention afforded is (in up to or) at least 15% better than placebo" and "wherein the level of infection and/or disease seen in the group is significantly lower than that which is seen with a placebo", respectively, i.e. these claims merely amount to a statement of the underlying problem. The technical features necessary for achieving this result should be added.

These specific result-to-be-achieved features have not been taken into consideration for the present examination of novelty and inventive step.

2.2 The requirement that the claims shall be clear applies to individual claims and also to the claims as a whole. In view of the differences in the scope of protection which may be attached to the various categories of claims, the wording of a claim leaves no doubt as to its category (c.f. **PCT Gazette-Section IV III-4.1.**).

However, regarding present **claim 5**, it is not clear whether it should relate to a use or a method type of claim.

item V

1 Reference is made to the following document(s):

D1 WO 01/17551 A (SMITHKLINE BEECHAM BIOLOG ;WETTENDORFF MARTINE ANNE CECIL (BE)) 15 March 2001 (2001-03-15)

D2 HPV Clinical Workshop & 20th International Papillomavirus Conference 2002, October 4-9, Paris, Institut Pasteur. Abstr.: P 099 Villa-L et al., A dose-raging safety and immunogenicity study of a quadrivalent HPV (type 6/11/16/18) L1 VLP vaccine in women. XP001156085

2 Novelty (Article 33(2), PCT)

2.1 Upon reconsideration, novelty objections concerning **claims 1-20** are no longer maintained, in view of the arguments provided by the Applicant.

This case would be a typical second medical use situation. Although patients with cervical cancers are reported to be infected by an average of 3.3 different HPV strains, there would still be a patient group where the cancer is not provoked by HPV-16 or -18. Thus, the use of the HPV-16/-18 vaccine for treating infection and/or diseases caused by non-HPV-16 or HPV-18 oncogenic HPV viruses has to be considered as separate medical indication.

Thus, the subject matter of **claims 1-20** would appear to be novel in the sense of **Art. 33(2), PCT**.

2.2 **D1** discloses a composition comprising HPV-16/18 L1 VLPs formulated with 3D-MPL and AlPO4 used for vaccination. **D1** also discloses the combination of said HPV vaccine with an hepatitis A or B virus antigen and/or herpes simplex virus antigen. Accordingly, a strong positive association between an HPV and human cancer is that which exists between HPV-16 and HPV-18 and cervical carcinoma. Other HPVs of particular interest are serotypes 31, 33 and 45.In addition to vaccination of persons susceptible to HPV infections, the vaccine may be used to treat patients suffering from said viral infections (c.f. abstract; p 1, §3; p 3, §3-5; p 8, last §; p 9, §4-5; p 10, §5; p 16, §3; example 1; claims 1-20).

The teachings of **D1** are considered to anticipate the subject matter of compound **claim 21**, as far as examined (c.f. item III, 2.1 above), in the sense of **Article 33(2), PCT**.

3 Inventive step (Article 33(3), PCT)

D1 is considered to be the closest prior art and discloses a composition comprising HPV-16/18 L1 VLPs formulated with 3D-MPL and AlPO4 used for vaccination. **D1** also

discloses the combination of said HPV vaccine with an hepatitis A or B virus antigen and/or herpes simplex virus antigen. Accordingly, a strong positive association between an HPV and human cancer is that which exists between HPV-16 and HPV-18 and cervical carcinoma. Other HPVs of particular interest are serotypes 31, 33 and 45.In addition to vaccination of persons susceptible to HPV infections, the vaccine may be used to treat patients suffering from said viral infections (c.f. abstract; p 1, §3; p 3, §3-5; p 8, last §; p 9, §4-5; p 10, §5; p 16, §3; example 1; claims 1-20).

The difference between the subject matter of **claims 1-20** and **D1** is that the HPV-16/-18 vaccine is used for the prevention of infection and/or disease caused by one or more of the group of oncogenic HPV types, the group excluding types HPV-16 and HPV-18.
The technical problem is to provide a further medical application of the known HPV-16/-18 vaccine.
The claimed solution is the use for the prevention of infection and/or disease caused by one or more of the group of oncogenic HPV types, the group excluding types HPV-16 and HPV-18.

As no prior art document convincingly points to a possible heterologous cross protection of the HPV-16/-18 vaccine, the subject matter of **claims 1-20**, as far as examined (c.f. point III above), would appear to involve an inventive step in the sense of **Art. 33(3), PCT**.

4 further comments

4.1 In a later European regional phase objections might be raised against any expression within the description such as "...incorporated by reference..." (e.g. on p 5, §1; p 11, §3; p 15, §2; p 17, §6) as the regional patent law requires that the application is self-contained.

4.2 The vague statement in the description on p 17, §2 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (**Article 6, PCT**) when used to interpret them (see also the **PCT-Gazette, Section-IV, III-4.3a**).

4.3 Abbreviations used within the claims, e.g. HPV, VLP, 3D-MPL should be spelled out at first occurrence, and then introduced by placing the abbreviation in parentheses after the term being abbreviated.

4.4 It would appear that contrary to the requirements of **Rule 5.1(a)(ii), PCT**, the relevant background art disclosed in **D1**, is not mentioned/discussed in the description, nor are

these documents identified therein.